Kawasaki Disease

ABSTRACT BOOK -

Oral Abstracts

ASSOCIATION OF SINGLE-NUCLEOTIDE POLYMORPHISM (rs1042579) IN THROMBOMODULIN GENE AND PLASMA THROMBOMODULIN LEVEL IN NORTH INDIAN CHILDREN WITH KAWASAKI DISEASE

Authors:

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Abstract

Objective:

Kawasaki disease (KD) is the commonest acute systemic vasculitis in children and predisposes to development of coronary artery abnormalities (CAAs). Thrombomodulin (THBD) gene polymorphism c.1418C>T (rs1042579) is associated with a high risk of cardiac-cerebral vascular diseases. However, association of THBD polymorphism (rs1042579) and plasma TM levels with susceptibility to KD and CAA formation is still unclear.

Methods:

Polymorphism in THBD gene (rs1042579) was analysed in 50 patients with KD and 50 age, gender and ethnicity matched controls using Sanger sequencing. Plasma TM levels were measured using an ELISA based assay.

Results:

Mean plasma TM levels (±SD) in patients with KD during acute phase was 2549.41 (±853.18) pg/ml and in control group was 2298.03 (±869.14) pg/ml. This difference was statistically significant (p= 0.042). Mean plasma TM levels in CC genotype was 2299.98 (±834.88) pg/ml and in CT/TT genotype was 2837.96 (±857.14) pg/ml. This difference was also statistically significant (p=0.005). Genotyping data did not reveal significant difference in patients with KD as compared to controls (p= 0.25), and in KD patients with and without CAAs (p = 0.407). Odds of finding a T allele in cases were 2.07 times greater than in controls (p = 0.093).

Conclusions:

This is first study from India, and second in the world, that investigates association of THBD gene polymorphism with KD. This is also the first study to assess plasma sTM levels in patients with KD. Our data show that plasma TM levels were significantly higher in KD patients with CT/TT genotypes. Further, the polymorphism rs1042579 at exon 1 of THBD gene was found to be more common in patients with KD than in controls but the difference was not statistically significant.

A Study On Effectiveness Of Infliximab Following IVIg For Reducing Coronary Artery Aneurysms

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Abstract

BACKGROUND:

Kawasaki Disease (KD) is emerging as the commonest childhood vasculitis in India, but because of late diagnosis many have coronary artery aneurysms (CAAs) at presentation. Both Infliximab (IFX) and corticosteroids have been proposed as add on drugs for patients with CAAs at diagnosis. This study was undertaken to assess efficacy of IFX in this context.

OBJECTIVES:

Determine effectiveness of IFX following IVIg on regression of CAAs.

METHODOLOGY:

This observational study was conducted at the Institute of Child Health Kolkata, India from January 2016 to December 2019. 33 children aged between 6 weeks to 7 years with KD received IFX after 1-2 doses of IVIg of which 15 received because of medium to giant CAAS at diagnosis, increasing CAA or developing new CAA following IVIg. Patients were analyzed in terms of change in size of CAAs on serial echocardiography done weekly x 4 weeks, monthly x 3 months and then every 3 to 6 monthly.

RESULTS:

15 children with CAAs received IFX, 7 with multiple/ giant CAAs at presentation and 8 with new or enlarging ones post IVIg. Seven of them were also IVIg resistant and 7 were infants, youngest being 6 weeks old. 4/15 had giant aneurysms and they were all infants. IFX was given at 5mg/kg within 24 to 48 hours of completion of IVIg infusion. Diminution in size was seen in 80 % (12 out of 15) cases on follow up, giant aneurysms being converted to medium or small sized aneurysms over 6 to 18 months. 50% reduction in the aneurysm size was noted in 60% (n=9) within first 6 months of administration.

CONCLUSIONS:

80% of children receiving IFX post IVIg showed progressive decrease in size of CAAs by 18 months.

A STUDY TO FIND MYOCARDITIS IN THE E.C.G.s OF KAWASAKI DISEASE

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Abstract

Objective:

1) To identify incidence of myocarditis through ECG changes in the acute phase of Kawasaki Disease
2) How ECG changes correlate with different acute inflammatory markers of blood in acute phase
3) The trend of resolution in ECG changes over time in 3follow ups(1,3 and 6 month).

Methods:

It is a hospital based case control observational study from January 2019 to January 2021 in which 83 Complete and 19 Incomplete cases are included and followed up 3times - at 1,3 and 6 months from the acute phage. 37 Covid KD phenotype cases were also included. In acute phase, all ECGs and blood investigation findings were compared with same number healthy individuals. Covid MISC patient and patient with known case of cardiac disease were excluded.

Results:

In our study ECG changes suggestive of myocarditis were found in a large portion of cases(88.8%) and that were 100% in Covid KD phenotype cases. The mean of QTc interval, QT dispersion, Tpeak-Tend dispersion were significantly higher in case group than normal healthy controls. Besides these Covid KD phenotypes also showed arrhythmia, ST elevation, deep Q wave significantly.When compare between Complete and Incomplete KD group the ECG abnormalities are more evident in Incomplete KD group .Overall coronary abnormalities were noted in 44% cases. NT-ProBNP, among the all inflammatory markers showed most significant correlations with QT dispersion and Tpeak-Tend dispersion. In the follow upto 6 months, most of the repolarization abnormality in E.C.Gs were persist.

Conclusion:

Evidence of myocarditis(88.8%) in KD is fur more than coronary involvement(42%). Moreover all Covid KD(100%)cases suffered from myocarditis. Ventricular repolarization were affected mostly. Abnormal ECG tracings were most significantly correlated with NT Pro-BNP. The more NT-ProBNP level in acute phase the more delay in resolution of ECG tracing during follow ups.

Abstract

RETROSPECTIVE ANALYSIS OF EFFECTIVENESS OF INFLIXIMAB BIOSIMILAR IN IVIG RESISTANT KAWASAKI DISEASE

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OBJECTIVE:

Determine effectiveness of Biosimilar of Infliximab (IFX) in IVIG resistant KD.

METHODOLOGY:

This retrospective study was conducted at Institute of Child Health, Kolkata from June 2020 to June 2021. 12 children aged between 6 weeks to 7years with KD received either IFX or its Biosimilar depending on the parents affordability, after 2 g/kg IVIG due to persistent fever and/or increasing coronary artery aneurysms (CAAs) . Patients were analyzed in terms of achievement of defervescence in hours, normalization of C-reactive protein(CRP) and improvement in echocardiography findings especially CAAs.

RESULTS:

Out of 12 cases, IFX was administered in 9 and the Biosimilar in 3. IFX was used in 1) IVIG resistant fever (4/9), 2) increasing CAAs post IVIG (2/9) and 3) overlapping indication ie. IVIG resistance with increasing CAAs (3/9). The Biosimilar was used in increasing CAAs post IVIG (1/3) and overlapping indication ie. IVIG resistance with increasing CAAs (2/3). Both IFX and the Biosimilar were administered at 5mg/kg. No adverse effects were observed.

All patients achieved defervescence within 24 hours with normalization of CRP by 48 hours. Diminution in size of aneurysms was seen in all cases on follow up. 2 cases with giant aneurysms received the Biosimilar and both had 50% reduction in the aneurysm size within first 6months of administration.

CONCLUSION:

The Biosimilar was effective in treating fever and normalizing CRP in IVIG resistant KD, and was also effective in reducing CAAs. Although this was only a small patient cohort, it showed efficacy similar to the original molecule at one third the price. So in the Indian Subcontinent, where cost of treatment plays a major role in decision making, a Biosimilar of IFX maybe considered if affordability is an issue.

Abstract

Characterization of endothelial dysfunction markers by flowcytometry and gene expression studies in Kawasaki disease patients from North India

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Introduction:

Kawasaki disease (KD) is a systemic, medium vessel vasculitis. Endothelial dysfunction is an important pathogenic event in cardiovascular diseases. The endothelium plays important role in vascular homeostasis. The initial inflammatory insult to the endothelium during the acute phase of KD leads to endothelial injury, while the persistent chronic & smouldering inflammation during the chronic phase leads to endothelial dysfunction.

Methods:

The present study is a single centre, prospective study in North India to assess endothelial dysfunction markers in KD patients and healthy controls. We propose to study KD patients diagnosed at different time intervals with and without coronary artery aneurysms (CAA) (Z score) according to American Heart Association (AHA) criteria 2004. Four groups were enrolled- Group 1: (diagnosed >6 months-1.5 years); Group 2: (diagnosed >1.5 - 3 years); Group 3: (diagnosed > 3 - 4.5 years) and healthy control. Estimation of circulating endothelial cells [CECs- (CD45dim/CD146+/CD31+/CD133-)] and endothelial progenitor cells [EPCs- (CD34+/CD309+ /CD133+)] was done by using specific antibody markers tagged with different fluorochromes, acquired on flowcytometer and analyzed using kaluza software. Percentage of CECs and EPCs were calculated by formula: %EPCs= Number of EPCs ´ 100/Number of mononuclear cells and % CECs = Number of CECs´ 100/Number of mononuclear cells .Quantitative gene expression analysis was carried out using real-time PCR.

Results:

Higher percentage of CECs (non-significant; $p>0.05$) was estimated in patients as compared to control group while significantly higher percentage of EPCs was found in KD patients than control. Gene expression studies reveals significantly higher ($p<0.05$) expression of CXCL8, leptin, VEGF-A, osteopontin in KD patients than control group while significantly lower expression of endogiln, and angiopoietin was found in KD patients. Expression of PECAM-1 and pentraxin3 was comparable in KD patients and age matched healthy controls.

Conclusion:

Cardiovascular complications are the major concern in KD. Acute inflammatory damage leading to functional and structural changes in coronary and systemic arteries, poses potential risks to KD patients during acute stage. The endothelial dysfunction in KD patients has been found to persist for several years after the acute stage and is a potential cardiovascular risk factor. Significantly elevated levels of EPCs and higher expression levels of CXCL8, leptin, VEGF-A and osteopontin was found in KD patients as compared to control. Percentage of CECs was found to be enhanced in KD patients compared to controls; however, this difference was not statistically significant probably due to small sample size.

"EVALUATION OF CIRCULATING MONOCYTE/ MACROPHAGE ACTIVATION MOLECULES BY ELISA IN ACUTE AND CONVALESCENT STAGES OF KAWASAKI DISEASE– A PRELIMINARY STUDY"

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Abstract

Objectives:

Kawasaki disease (KD) is an acute, self-limiting, febrile illness with unknown etiology. Diagnosis is based on clinical symptoms and signs. Despite more than 5 decades extensive research, the exact etiology of KD is unknown. Significant monocyte infiltrates in affected vessels were documented in histopathological studies. It indicates monocyte activation molecules may have role in recruitment of monocytes and their activation in acute KD. We investigated 3 different monocyte activation markers- sCD14, sCD163 and CCL2/MCP-1 (monocyte chemotactic and activation factor) in children diagnosed with KD.

Methods:

We analyzed plasma levels of monocyte activation markers- sCD14, sCD163, MCP-1/ CCL2 in 16 children with KD who were admitted in Post Graduate Institute of Medical Education and Research, Chandigarh between January 2019 to December 2020. We measured in patients with KD, febrile and healthy controls by using commercially available Quantikine® ELISA kits (R&D Systems® USA) in a fully automated ELISA machine (Infinite200 pro) and the results were read in the ELISA reader (Tecan). We compared the molecules before, after IVIg treatment, convalescent phase and with febrile and healthy controls.

Results:

Plasma median sCD14 levels were higher in febrile controls 2754.10 (2249.50-3226.74) ng/ml, compared to children with acute KD 2228.84 (1899.34-2425.22) ng/ml and healthy controls 2252.64 (1375.07-2737.17) ng/dl (p-value 0.038). There was no significant difference in sCD163 values between cases, febrile, and healthy controls. Median CCL2 levels were highest in children with KD 318.85 (184.29-449.23) pg/ml, however, the difference was not statistically significant between cases, febrile, and healthy controls (p-value 0.075). Levels of CCL2 significantly dropped after IVIg infusion in children with KD (p-value 0.47). No significant fluctuations in levels of sCD14 and sCD163 over time in children with KD. Levels of CCL2 were higher in children with CAAs, however, the difference was not statistically significant (p-value 0.082).

Conclusions:

Our results suggest that acute phase of KD have significantly elevated CCL2 levels and there was significant response with IVIg treatment, which indicates that CCL2 may contribute to monocyte mediated inflammation and cardiovascular damage in KD.

Proposal for a Scoring System to Predict the Risk of IVIG Resistance in Indian Children with Kawasaki Disease

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Abstract

OBJECTIVE :

To propose an independent Indian scoring system to predict the probability of IVIG resistance in Kawasaki Disease (KD) for the native population, based on the various Japanese risk scoring systems.

METHODS :

Prospective observational study in which clinical and laboratory parameters of 70 children with KD, treated with IVIG, admitted at Institute of Child Health, Kolkata from January 2019 to April 2020 were tabulated along with their response to IVIG. Recrudescent or persistent fever after >36 hours of completion of IVIG therapy was taken as IVIG resistance. Based on the relevance of the existing Japanese scoring systems and correlating the various clinical and lab parameters to IVIG response in our cohort, an Indian scoring system was formulated.

RESULTS:

I. Amongst 70 children included in the study, 22 (31.4%) were non responders to IVIG .

II. High Kobayashi score (p value = 0.0009), high Egami score (p value =0.0106) and high Sano score (p value = 0.0262) were all significantly associated with IVIG resistance. Sano score had the highest sensitivity (81.8%) and Kobayashi score had the highest specificity (77.1 %) in our cohort.

III. Based on the findings the following scoring is proposed:

Criteria	Value	Score
Age	<=12 months	1
Platelet Count	<3 lacs/cmm	2
Total Bilirubin	<=0.9mg/dl	2
CRP	>=70 mg/L	1
AST	>=200 IU/L	2

A score of >=4 has a significant association with IVIG resistance.

CONCLUSION:

An independent Indian scoring system is being proposed that needs to be validated by further studies.

Abstract

Infection and Kawasaki disease: An analytical study from North-India

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Background and Objective:

Kawasaki disease (KD) is the most common vasculitis in children. The etiology of KD remains an enigma despite more than 50 years of extensive research. However, multiple lines of evidence have supported the role of infections as possible triggers for KD. It is believed that KD develops in a genetically susceptible host on exposure to an environmental agent that is most likely an infectious agent. Aim of this study is to report various infections identified in a cohort of patients with KD at the Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Methodology:

We carried out a review of case records with KD during 1994-2019. Of 950 cases of KD during this period, 102 children had some evidence of infection during the course of their illness. This subgroup of patients was subsequently analyzed in detail.

Result:

Overall 10.73% children had evident active infection during the course of KD. Of 102 children (67 boys), majority (68/102; 66.6%) was diagnosed as incomplete KD. Mean delay in diagnosis was 11 days (range 4-35 days). Only 1 sibling developed KD at the same time. Fever was present in all and periungual peeling was seen in 98 (96%%) patients. Microorganisms were isolated in 72 children (70.5%) that were bacteria (n=52); virus (n=15); fungus (n=4); protozoa (n=1). Superficial and deep-seated abscess was most common infective features (28/102; 27.45%). Other clinical features were pneumonia (n=27), gastrointestinal manifestations (n=26), shock (n=9), blood stream infection (n=5), urinary tract infection (n=4), splenomegaly (n=8) and arthritis (n=9, septic arthritis 2). Amongst the bacterial etiology, while staphylococcus and streptococcus were frequently encountered, dengue virus was commonest amongst viruses. Neutrophilic leukocytosis (86/102; 86.27%) was most commonly noted amongst supportive laboratory criteria followed by thrombocytosis (76.2%), anemia (62.5%), hypoalbuminemia (59.8%), hyponatremia (50%) and transaminitis (26.4%). Sterile pyuria was noted in 7 (5.83%) children. Ninety-six children were treated with first dose of IVIg (2gm/kg) and 5 required adjunctive therapy (2 received second dose of IVIg and 3 received both infliximab and steroids) along with low dose aspirin. Coronary artery abnormalities (CAAs) were seen in 12 (11.7%) patients during acute phase, which became normalized with in first 6 weeks in all patients. One child had myocarditis and succumbed to his illness.

Conclusion:

Based on these results it may be concluded that approximately one tenth of all children with KD may be associated with an infection in our set up and mostly it presents as incomplete KD. This infection may be a possible trigger for the disease. One should not exclude the diagnosis of KD even if there is an evidence of infection.

Abstract

Hemodynamically significant Brady arrythmias complicating MIS-C – A case series

Authors:

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Objective:

MIS-C, a hyperinflammatory state in children, temporally linked to COVID, is well known for cardiac complications like myocarditis, Left ventricular dysfunction and coronary aneurysms. However, high grade, hemodynamically significant brady arrythmias requiring pacing support is largely unknown. Hence mindful anticipation and monitoring is quintessential in preventing mortality.

Methods: Here we describe three cases of MIS-C, who presented with complete heart block, requiring pacing support, from 2 tertiary care centers in India. Clinical data were collected from medical records, after obtaining informed consent from guardians.

Results:

Our first case was a 3-year-old female child who presented with 2 days history of fever, gastro-intestinal symptoms, respiratory distress and shock. She had grade II Atrio-ventricular block, dilated left heart chambers with left ventricular systolic dysfunction and mild elevation of CRP 3.32 mg/L. Our second case was a 3-year-old female child, who presented with 1 day history of fever, convulsions, respiratory distress and shock. She had ventricular escape rhythm, severe left ventricular dysfunction and normal coronaries with CRP of 14.28 mg/L.

Our third case was a 10-year-old girl, who presented with fever, muco-cutaneous vasculitis, gastro-intestinal symptoms, convulsions, respiratory distress and shock. She had complete heart block, systolic dysfunction and normal coronaries, with CRP of 15mg/L.

All our cases received IVIg, pulse methyl prednisolone, temporary pacing support as per standard protocol. First child succumbed to her illness and other two children required permanent pacemaker implantation in view of persistent complete heart block despite resolution of hyperinflammatory state.

Conclusion:

High grade hemodynamically significant brady arrythmias can complicate MIS-C and can be potentially fatal without timely intervention. Our cases were unique in that, arrythmias developed early in the course of the disease with only mild elevation in inflammatory markers, causing death in 1 and need for permanent pacing support in other two.

4th Annual Conference of Indian Society of Kawasaki Disease abstract submission format

Anticoagulation in children with Kawasaki disease: our experience at Chandigarh, North India

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Abstract

ABSTRACT:

Title: Anticoagulation in children with Kawasaki disease: our experience at Chandigarh, North India

Objective:

To describe safety and efficacy of antiplatelet and anticoagulation therapy (aspirin and low molecular weight heparin (LMWH)/warfarin) in a cohort of Kawasaki disease (KD) patients with moderate to giant coronary artery aneurysm.

Methods: Records of all children diagnosed to have KD during 1994-2020 were analyzed. Of the 1076 patients with KD, clinical details of children who had received aspirin and either LMWH/warfarin were retrieved.

Results:

Thirty-eight (3.53%) children (28 boys; 10 girls) with KD, were put on aspirin and LMWH/warfarin. Median age of diagnosis was 18 months (range 1.5 months-12 years). Ten children (26.3%) were <1-year age at diagnosis. Twenty-seven patients (71%) have received LMWH, while 18 (47.4%) received warfarin. Five patients received initially LMWH for 12-31 months duration followed by oral warfarin. Giant aneurysms were present in 35 patients while 3 patients had moderate sized aneurysms. Thromboses developed in acute phase of disease in 4/38 (11.4%) and most common coronary artery affected was LAD. All patients were continued on oral aspirin (3-5 mg/kg/day) along with anticoagulation therapy and 5 patients also received a second antiplatelet agent (clopidogrel). Median duration of LMWH was 14 months (range: 3-32 months), and median warfarin duration was 42 months (range: 2-126 months). In 18 patients we were able to monitor factor Xa activity and median activity was 0.46 IU/mL (0.32-0.81). Median INR in patients receiving warfarin was 1.55 (0.99-2.73). There were no significant complications related to anticoagulation in any of the patients, although parents frequently complained of local bruising. Serial 2D-echocardiogram during follow-up showed remodeling of coronary arteries. None of the patients developed thrombosis or symptomatic stenosis during follow-up. Duration of follow-up was 1414 patient-months.

Conclusion:

Although the recommended INR in patients with KD and large aneurysm who are receiving anticoagulation therapy is 2-3, we maintained our patients on lower INR. Our results show that even on a much lower INR, these children have had no significant complications.

Kawasaki Disease

ABSTRACT BOOK -

Poster Presentation

A novel biomarker in predicting coronary artery lesions in Kawasaki disease

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Introduction:

Coronary artery lesions (CAL) are specific feature of Kawasaki disease (KD) which develops during the second week of illness. The diagnosis of KD, especially incomplete form, is made utilising non-specific clinico-laboratorial criteria which is often met by iron deficient children of our population presenting with tropical infection. This clinical dilemma forces clinicians often to diagnose KD only after the development of CAL. Specific biomarker in addition to existing criteria will facilitate early diagnosis and predict the development of CAL. Hence, this study was carried out to determine whether Neutrophil: Lymphocyte ratio (NLR) at admission can predict CAL development.

Method:

This was a retrospective record-based study, where 79 consecutive KD patients were enrolled from 2015-2020.

Results:

The median (IQR) age of presentation was 3(1,5) years. Incomplete KD was observed in 62% children. The median duration of presentation and IVIg administration from the onset of fever were 5(4,8) and 7(6,10) days respectively. CAL developed in 44 (55.6%), out of which 34 (43.03%) had coronary artery aneurysm and 10 (12.6%) had coronary artery dilation. Thirteen patients had IVIg resistance. The NLR at admission of all patients were 2.2(1.5,4.1). Comparison of the groups with and without CAL in terms of demographic and clinical variables revealed that patients with CAL had significantly higher proportion of conjunctivitis, IVIg resistance, higher NLR, platelet lymphocyte ratio (PLR). On performing multivariate analysis, NLR at admission was found to be significantly associated with CAL. Receiver operator curve (ROC) revealed an NLR-cut off of 2.08 at admission to be 82% sensitive and 80% specific in predicting CAL [AUC = 0.85 (95%CI 0.75-0.94; p-value$<$0.001)].

Conclusions :

NLR can be used for predicting CAL and facilitate early diagnosis of KD. NLR $>$ 2.08 at admission was observed to provide 2 days lead time in diagnosing KD in our population. These findings need to studied prospectively among all febrile children to understand its predictive capacity to diagnose KD.

Flow cytometry based assessment of early and late monocyte activation in children with Kawasaki disease - a preliminary study

Authors and affiliation:

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ABSTRACT

Objectives :

To study monocyte activation markers in Kawasaki disease (KD) as compared to healthy and febrile controls and to determine whether intravenous immunoglobulin (IVIg) leads to decrease in monocyte activation markers in patients with Kawasaki disease.

Methods :

We studied different populations of monocytes (Classical [CD14+CD16-], intermediate [CD14++CD16+], and non-classical [CD14+CD16++] monocytes) and also early (CD69) and late (HLA-DR) activation markers of monocytes in 11 North-Indian children with KD between January 2019 and December 2020 in a tertiary care hospital and compared them with healthy and febrile age-matched controls using flow cytometry. The activation markers were also assessed in follow-up in children with KD to see the response of IVIg on monocyte activation.

Results :

Children with KD during acute stages, had higher absolute numbers of classical and intermediate monocytes as compared to healthy controls however, it was statistically significant only for intermediate monocytes (p-value 0.013). Absolute numbers of CD14+ having CD69 expression were significantly higher in cases and febrile controls as compared to healthy controls (p-value 0.001). Significantly higher absolute counts of CD14+ monocytes having HLA DR expression were seen in acute KD as compared to healthy controls (p-value 0.019). Absolute counts of classical and intermediate monocytes were higher in acute KD and it progressively decreased in follow up samples. CD69 expression was significantly more in all the subpopulations of monocytes in acute KD as compared to follow up samples. Absolute counts of classical and intermediate monocytes having HLA-DR expression were significantly higher in acute KD as compared to follow-up samples (p-value 0.007).

Conclusions :

We documented increase in CD14+ monocytes during acute phase of KD that normalised in follow-up. We also documented an activated status of both classical and intermediate monocytes in acute phase of KD that subsided in follow-up. Our results suggest IVIg may decrease monocyte activation in KD, thereby controlling systemic inflammation.

Kawasaki Disease Lingering Around Common Gastrointestinal Symptoms: A diagnostic conundrum

Authors:

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ABSTRACT

Objective:

Kawasaki disease (KD) is the commonest childhood vasculitis. Gastrointestinal (GI) symptoms can occasionally be forerunner of KD and may pose a diagnostic challenge to treating physicians. There is paucity of literature on GI presentations of KD. To evaluate KD children with predominant GI presentations.

Methods:

We analysed case records of all children with GI presentations of KD during January 1994-April 2021.Diagnosis of KD was based on American Heart Association criteria(AHA).

Results:

We diagnosed 1078 children with KD during study period. Of these, 24 (19 boys; 5 girls) had a GI presentation. All had GI symptoms during acute phase of disease. Median age at diagnosis was 3.5 years (range 4 weeks-13 years). Manifestations included acute gastroenteritis(n=8); blood in stools(n=3); upper gastrointestinal bleed(n=1); subacute intestinal obstruction and intussusception(n=2); colitis (n =3); mesenteric mass(n=1), ulcers in colon(n=1); gall bladder perforation(n=1); jaundice(n=7) and acute fulminant liver failure(n=1). Delays in diagnosis ranged from 7 days-4 weeks. Twenty children responded to single dose of IVIg (2g/Kg);3 children required a second dose of IVIg; infliximab was given in one case. 2-D echocardiography revealed normal sized coronary arteries in 21 patients. One patient with acute fulminant liver failure had left main coronary artery(LMCA) aneurysm (2.8mm;+2.7z) and macrophage activation syndrome. He succumbed to illness. One patient with jaundice had multiple aneurysms (LMCA= 6.17 mm (+7.42); LAD=4.68mm(+6z); RCA= 7.5mm (+10.63Z)); another had right coronary artery dilatation (4.2 mm).

Conclusions:

None of the GI manifestations are part of AHA criteria. GI presentation of KD is uncommon and may create diagnostic confusion for the internist. Children with GI manifestations appear to have more severe forms of KD.

A Study On Cardiac Evaluation In Multisystem Inflammatory Syndrome in Children (MIS-C) associated with SARS COV 2

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ABSTRACT

Introduction:

MISC is a multisystem disease but predominantly affects the heart causing sudden severe myocarditis, shock and coronary artery aneurysms(CAA).

Methods:

Patients satisfying WHO MISC criteria admitted at Institute of Child Health, Kolkata, India between July to December 2020 were included. All were evaluated clinically and by Echocardiography at admission and post treatment. Follow up echocardiography was done at 2weeks, 6 weeks, 3 and 6 months. Treatment protocols and outcomes were noted down.

Results:

71 patients with a median age of 11 years (IQR 3 years) were admitted. Intensive care (PICU) admission was needed by 45% and 29.5% required inotropic support. Cardiac affection was present in 57.74% (n=41) mostly as myocarditis (disproportionate tachycardia, ECG and echocardiographic changes) of which 29.5% had low ejection fraction (EF 40 to 47%).

NT- Pro BNP and CRP was significantly higher amongst patients with cardiac affection; >935.7 pg/ml and > 99.55 mg/L at admission respectively might act as a guide as to the need for aggressive management.

19 children (26.7 %) had CAA (Z score> +2) and Kawasaki Disease like manifestations. 4 had LAD dilatation (mean+3.18Z),3 LMCA dilatation (mean +2.51Z) and 4 had both (mean LMCA +3.57Z and LAD +3.31Z). 2 patients had multiple CAA involving LAD, RCA, LMCA. 1 had only RCA dilatation(+2.87Z).

91.5% received IVIg, mostly at 2g/kg. Methylprednisolone (MP)only was given to 4 and 40 (56.3%) received pulse MP 10-30mg/kg/day x 3 to 5 days + IVIg.

EF improved by 48 to 72 hours of initiation of therapy. Patients presenting with shock, requiring inotropes, received MP + IVIg. On follow up, 89.5% patients with CAA's had regression by 6 weeks and rest over next 6 months.

CONCLUSION:

Acute myocarditis with or without CAA is the predominant cardiac affection in MISC. Early identification and aggressive therapy reverts it rapidly without significant residual lesions.

Multisystem Inflammatory Syndrome in Children (MIS-C)- Our experience from Chandigarh, North India

Authors:

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ABSTRACT

Background/Objective:

Multisystem inflammatory syndrome in children (MIS-C) is a hyperinflammatory syndrome following severe acute respiratory syndrome coronavirus 2 (SARS Cov-2) infection. This study aims to analyze the epidemiological and clinical profile of MIS-C patients with emphasis on cardiovascular involvement.

Methods:

We analyzed 46 children with MIS-C admitted to our unit from October, 2020 to October, 2021. WHO MIS-C criteria were used for diagnosis. We collated the demographic details, clinical features, laboratory parameters, treatment, and outcome of children with MIS-C with special emphasis on cardiac involvement.

Results :

Forty six children were admitted with diagnosis of MIS-C (n=46) to our unit. Median age of our cohort was 5 years (Range: 4 mo-15 years) with male: female ratio of 2.8:1. Predominant manifestations at presentation were fever (95.6%), rash (71.7%), eye changes (60.8%), mucosal changes (52.2%), gastrointestinal symptoms (vomiting/diarrhea) (58.7%) and shock (26%). History of covid exposure was present in 36.9% and 73.9% were positive for SARS Cov-2 serology.

PICU admission was required in 28.3% of the patients and 15.2% needed inotrope support. Cardiac abnormalities detected by 2D Echocardiography were low ejection fraction in 8.6% (4/46) and coronary artery dilatation in 10.8% (5/46) of children. CT-angiography was done in 5 patients (10.8%) and it showed pancoronary dilatation (LMCA, LAD and RCA) in 2 children (4.3%). While intravenous immunoglobulin (IVIg) alone was used in 19.5% of the patients, only steroids was used in 4.3% of the patients. Both IVIg and Steroids were used in 71.7% of the patients and infliximab was used in 4.3%. One mortality was reported in this cohort.

Conclusion :

MIS-C is a multisystem hyperinflammatory syndrome with significant cardiac involvement. Although 2D-echocardiography is useful in initial detection and follow-up of cardiac involvement, CT-angiography can be used as an important diagnostic tool for better delineation of coronaries.

Kawasaki Disease with Peripheral and Facial Gangrene

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ABSTRACT

Introduction

With onset of SARS-CoV-2 pandemic, Kawasaki Disease (KD) has come back in focus with its many atypical manifestations. Presence of gangrene, severe atypical dermatological features, fever and raised inflammatory markers in a child should prompt the clinician to consider diagnosis of KD.

Case Details

We present a three-and-a-half-year-old male child who presented with fever for 5 days along with extensive gangrene of all 4 limb and face and purpura fulminans. The child was diagnosed as incomplete KD based on clinical & laboratory criteria as per AHA 2017 guidelines. This case highlights very severe form of Kawasaki disease requiring IVIG, pulse steroids as well as infliximab for adequate control and complete resolution of the disease.

Results

The child was successfully treated with complete resolution of gangrene and no facial scarring.

Conclusion

Though peripheral gangrene is reported in infants, Kawasaki disease must be thought of as a differential diagnosis even in older children who present with extensive gangrene.

Gangrene in childhood may be added as a standalone diagnostic criterion for KD.

Even with initial normal coronary artery SD scores, we must use biochemical markers to diagnose incomplete KD. As per AHA 2017 guidelines, delta change of more than 1 SD score on follow may indicate coronary artery dilatation in retrospect, as in our patient

A retrospective analysis of the need for methylprednisolone in addition to ivig for treating covid-19 associated multisystem inflammatory syndrome in children (mis-c).

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ABSTRACT

Objective:

To retrospectively analyse the treatment to decide on need for methyprednisolne (MP) in addition to Intravenous Immunoglobulin (Ivlg)

Methods:

71 patients admitted between July and December 2020 in Institute of Child Health, Kolkata and satisfying the WHO MIS-C were included. We retrospectively analysed the treatment data to decide on the need for methylprednisolone (MP) in addition to intravenous immunoglobulin (Ivlg). Since CReactive Protein (CRP) and Echocardiography are done in all, and myocarditis was the commonest cardiac affection; Ejection Fraction (EF) along with CRP was used for the analysing data.

A logistic regression model was fitted to the data to classify MP usage based on CRP and EF. A chi square test of dependence was carried out to test dependence of EF on MP administration.

Results:

57.74% (41) children had myocarditis, 30.9% had low EF. 30.9% (22) received Ivlg only, 60.6% (43) received Ivlg and Methyl Prednisolone, 8.5 % (6) received steroid only.

Based on logistic regression model to classify MP administration according to CRP and EF (reduced or normal), coefficient for CRP had a p value >0.05, signifying it does not significantly affect MP requirement. However, coefficient for EF had a p value <0.05, which means that EF has a significant relation to MP administration, and a change in EF value from normal to reduced will change the probability of MP requirement

	EF Normal (>55)	EF Reduced (<55)
MP: NO	25	3
MP: YES	24	19

24 children with normal EF were given MP and Ivlg, and 25 were not. 19 children with reduced EF (<55) received MP and Ivlg whereas 3 did not. To statistically test this dependence of MP administration on EF values, we carried out the chi square test of dependence of categorical values. The test gave a p value <0.05, which means that there is a relation between EF (reduced/ normal) and MP administration.

CONCLUSION: Patients with low EF will require MP in addition to IVIg; irrespective of CRP values.

Atypical Presentation of Multisystem Inflammatory Syndrome in Children

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ABSTRACT

Objective :

we describe a case of Post COVID persistent fever, diarrhoea and diffuse small bowel inflammation, suggesting an atypical presentation of MIS-C

Methods :

A nine-year-old boy presented with 2 months history of recurrent diarrhea, vomiting, pain abdomen, low grade fever, and weight loss of 6 kg. Past history was significant for having mild acute COVID 19 infection 2 months prior.

He was investigated thoroughly for these symptoms in multiple centres.Hemoglobin was 9.7 g/dl, elevated ESR (37 mm) and thrombocytosis of 4.7 lakhs/cu.mm were noted. Ultrasonogram of abdomen showed small abdominal lymphadenopathy, Upper GI endoscopy showed fundal gastritis, duodenitis, and biopsy of D2 showed mild inflammation of the duodenum. colonoscopy was normal. CT abdomen showed small mesenteric lymph nodes. Mantoux test and TB Quantiferon Gold were negative.

On examination, he looked emaciated, and had few small cervical lymph nodes palpable. Other systemic examination was normal. he continued to have evening spikes of fever of 100 - 101^{0} F during hospital stay. Blood cultures were sterile, Procalcitonin and 2D Echo were normal. A whole-body PET CT done as a part of PUO work up showed diffuse thickening and enhancement of appendix, diffuse increased FDG uptake in entire small bowel loops with wall thickening and mucosal enhancement in duodenum, jejunal and ileum.

Biopsy of ileum was recommended but the family refused. With TB workup negative, a possibility of atypical presentation of MIS-C was considered. He had a prolonged course as opposed to the acute presentation commonly seen in MIS-C and satisfied only 1 clinical criterion with Gastrointestinal symptoms. But other criteria of lab evidence of inflammation, infections ruled out and history of COVID 19 RT PCR positive supported the diagnosis.

Results: he was given a course of low dose steroids and responded well.

Conclusion:

While classical Kawasaki and MIS- C are well known, atypical presentations should still be considered as part of the spectrum to help managing these cases.

MISC : A comparative analysis of the 1ST &2ND waves

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ABSTRACT

INTRODUCTION:

Multisystem Inflammatory Syndrome in Children(MIS-C)is a newly described hyperinflammatory syndrome occurring 2 to 8 weeks post Covid. The first MIS-C wave hit Bengal around July 2020 and lasted till January 2021. The 2nd wave started brewing in April and went on till July 2021.

OBJECTIVE:

The following study is a comparative analysis between the 2 waves.

METHODOLOGY:

Single centre study with patients who fulfilled the WHO MISC criteria. Clinical presentations, echocardiographic features, treatment protocols and outcomes were noted.

COMPARATIVE RESULTS:

	2020 (n=75)	2021 (n=48)
Median Age	11 yrs	6.16 yrs (<2 yrs age= 8 patients)
History of COVID positivity	42.5%	68.75%
Rashes	86%	39.5%
Abdominal symptoms	70%	40%
Only febrile phenotype	3	13
Myocarditis	28.7%	39.5%
Coronary Artery Dilatations	29.5%	47.9%
PICU admission	45%	58.3%
Deaths	Nil	3 (1= MAS, 2=refractory myocarditis and hypotension)
TREATMENT GIVEN:	**2020**	**2021**
IVIG 38.7%	Nil	
IVIG + steroids	56.3%	66.6 %
Only steroids	5 %	29.1%
BiologicsNil	3 Infliximab	

CONCLUSIONS:

The 2nd wave was shortlasting but more intense affecting a higher number of younger children, with increase in only febrile phenotype and Kawasaki disease like presentations. Whereas majority of 1st wave children had abdominal symptoms and rashes, the numbers almost halved with the 2nd. There was higher propensity of cardiac affection and need for PICU admission. Use of upfront steroids increased and only patients with myocarditis and Kawasaki like presentation received IVIG. Infliximab was used in 3 refractory cases and there were 3 deaths.

ANALYSIS OF THE EPIDEMIOLOGICAL AND CLINICOPATHOLOGICAL CHARACTERISTICS AND TREATMENT MODALITIES IN MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) PATIENTS: AN EASTERN INDIAN COHORT

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ABSTRACT

OBJECTIVE :

To document and analyse our experiences from eastern India pertaining to multisystem inflammatory syndrome in children (MIS-C) which is a novel disease entity with variable presentations and varying treatment guidelines.

METHODOLOGY :

Cohort study on children diagnosed with MIS-C by the WHO criteria at Institute of Child Health Kolkata from July to December 2020. History, clinical findings, laboratory investigations including imaging, response to different therapeutic modalities and post discharge follow up data were recorded and subsequently analysed.

RESULTS :

75 children with median age 11 years (IQR 3 years) were included. All presented with fever. 86% had erythematous maculopapular rashes. Gastro-intestinal complaints were present in about 30%. Central nervous system affection varied from extreme irritability in 63% to drowsiness in 18%. Intensive care admission was needed by 45% and 29.5% required inotropic support. Cardiac affection was detected in 57.74% mostly as myocarditis and 27% had coronary artery dilatations. 20% required respiratory support and 4 had to be ventilated. Significant laboratory investigations included neutrophilia, very high CRP (mean 186.8mg/L) and NT-proBNP (mean 9141 pg/ml). COVID IgG was positive in 91%.[3]

91.5% received IVIg and 56.3% received methylprednisolone(MP) + IVIg. Dosage of MP varied from 2 to 30mg/kg, doses were individualised depending on the clinical severity. All of the patients survived and had normalisation of cardiac lesions on followup.

CONCLUSION :

MIS-C is a hyperinflammatory disease with variable presentations often requiring intensive care management. Early identification and immediate administration of steroids/ IVIG reverts the stormy progression, usually without significant residual morbidity.

Incomplete Kawasaki Disease with Intravenous Immunoglobulin resistance presenting as myositis in a three-year-old boy- a case report

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ABSTRACT

OBJECTIVE :

Reporting a boy with atypical resistant Kawasaki disease presenting with myositis as the presenting complaint

CASE :

A 3-year-old male child presented with pain in both lower limbs with refusal to walk followed by fever on day 3 of illness. On examination, the boy was crying and resisting even slight movement of limbs, but there was no evidence of any signs of inflammation such as warmth, erythema, or swelling on any joints. There was no rash; general examination and systemic examination were normal. Investigations revealed an elevated total leukocyte count and inflammatory markers. A provisional diagnosis of osteomyelitis was made and started on Inj. Cloxacillin empirically. X-ray and USG of the lower limbs were unremarkable. No evidence of osteomyelitis was noted on the bone scan, but MRI revealed myositis of bilateral quadriceps, with no bony or other soft tissue abnormality. On 7th day of hospitalization, pain and fever persisted, but the child developed periungual peeling. Atypical Kawasaki disease was suspected which was confirmed after noting an increasing trend in inflammatory markers, and an echocardiogram showing coronary dilatation. Intravenous immunoglobulin (IVIg) and aspirin were started, but the child continued to have fever even after 72 hours of IVIg. Other possible etiologies like leukemia, multisystem inflammatory syndrome in children (MISC), acute rheumatic fever, and vasculitis were actively sought after and ruled out. In view of persisting fever, pain and elevated inflammatory markers the child was given the second dose of IVIg following which there was defervescence of fever, decrease in the inflammatory markers, and the child was able to walk and pain-free. The follow-up echocardiogram revealed persistence of coronary artery abnormality and was started on dual antiplatelet therapy and is under follow up.

Conclusion:

Incomplete KD can closely mimic many diseases and can present with several atypical symptoms; myositis with diffuse bilateral lower limb pains may be one among them. A high index of suspicion is essential throughout the course of any febrile illness so that the a diagnosis of incomplete KD is made without any undue delay.

Kawasaki disease at a tertiary care center in South India – A Single Centre Experience Over 5 years

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ABSTRACT

Introduction :

Kawasaki disease (KD) is the most common cause of acquired heart disease in developed countries. KD is increasingly being reported from India; however, studies involving a large number of patients are sparse.

Objective :

To study the profile of patients diagnosed with KD at a tertiary care center in South India.

Methods :

All children presenting to the center from Feb 2017 to October 2021, diagnosed to have KD, were retrospectively included in the study. Clinical and laboratory profiles, including echocardiograms, were reviewed. Factors contributing to intravenous immunoglobulin (IVIg) refractoriness and the development of coronary artery abnormalities (CAA) were assessed.

Results :

A total of 50 children with KD presented to the center during the study period. While 42 received initial treatment at our center, eight were referred after the initial IVIg infusion for refractoriness to treatment and/or persistence of CAA (n=7) or pre-existing X-linked agammaglobulinemia (n=1). These children were not included in the analysis of clinical and laboratory features on presentation (Table 1). The age range was 2 months to 11 years (mean age was 3.1 years). More than two-thirds of the cohort was male (n = 33/50). Mucosal involvement was the commonest clinical abnormality for the group, followed by rash.

Twenty two children had complete and 20 had incomplete KD. Twelve out of 20 incomplete KD cases were infants. A total of 20 out of 50 children (40.8%) had CAA. The left main was the commonest coronary artery to be involved (n = 15), followed by left anterior descending (n = 9) and right coronary artery (n = 7).

Infants had a more severe disease profile. Cardiac involvement was higher in infants (8/16 had CAA vs 6/26). Infants also manifested atypical features such as upper limb arterial thrombosis ,liver derangement and lower motor neuron facial palsy. The association of clinical features and laboratory values on presentation with coronary artery involvement, is summarized in Table 1.

A total of 10 children in the cohort were refractory to treatment (20%) and CAA was present in eight of them. Of the children refractory to IVIg, five received infliximab, three received methylprednisolone, while two received both infliximab and methylprednisolone. On follow- up, three patients had persistence of aneurysm.

Conclusion :

A significant proportion of infants with KD had cardiac involvement. Infants were more likely to have IVIg-**resistant disease.**

Clinical features	With CAA (n=14)	Without CAA (n=28)
n (%) Age <12 months	8/14 (57)	8/28 (28.5)
Gender		
Male	8/14 (53)	17/28 (60.7)
Female	6/14 (42.8)	11//28 (39.2)
Eye signs present	12/14 (85.7)	17/28 (60.7)
Mucosal changes present	14/14 (100)	24/28 (85.7)
Lymphadenopathy present	6/14 (42.8)	8/28 (28.5)
Extremity signs present	7/14 (50)	16/28 (57.1)
Rash present	13/14 (92.8)	24/28 (100)
Mean days of fever	10.4	9.4
CRP (mg/L)	63.9	67.2
ESR (mm at end of 1st hr)	74.9	60.8
Platelet counts (x 109/L)	6.8	5.1
TLC (×109/L)	15.4	14.3
Hemoglobin (g/L)	9.5	10.8

Profile of Multi System Inflammatory Syndrome in Children related to COVID19 - A Multi-centric study from South India

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ABSTRACT

Introduction:

Multisystem Inflammatory Syndrome in Children (MIS-C) is a severe complication of SARS COV-2 infection associated with significant morbidity and can be fatal if left unrecognised.

Objectives

To evaluate the clinical profile of children admitted with MIS-C associated with SARS-CoV2 infection.

Methods

A retrospective multi-centric study was carried out at five tertiary care centres in South India. Cases of MIS-C diagnosed during October 2020 – September 2021 were included. Diagnosis of MIS-C was based on WHO criteria. All children underwent echocardiography at admission, discharge, and 4-6 weeks of follow-up. We also compared younger children (<5 years of age) with older ones to determine if age at presentation could predict severity in children with MIS-C.

Results

A total of 81 children were diagnosed to have MIS-C during the study period. Mean age of presentation was 6.8 years. Males were predominantly affected (70.3% vs 29.6%) in our study population. Table 1 represents the important demographic and clinical features of the patients in our study. In our study, 4/81 (4.93%) had COVID RT-PCR positive, 61/81 (75.3%) had positive COVID serology and 22/81 (27%) had positive contact history of patients with COVID in the last 2 months prior to the appearance of symptoms.

The most common clinical presentation in our study other than fever was red eyes (54.3%), rashes (54.3%) and pain abdomen (65.9%) followed by lymphadenopathy (24.6 %). 29.6% of the children had shock at admission and 27.1% of them had myocardial dysfunction. Average duration of PICU stay was 6.6 days. Children with high NT-proBNP had more severe presentation. Hypotension was more common at presentation in older children (>5 yrs) as compared to younger children (< 5yr), however, it was not found to be statistically significant ($p < 0.09$).

Most children were treated with IVIG, and steroids (66.6%) and all children responded promptly to treatment. One child required treatment with Tocilizumab (1/81) and Anakinra was used to treat 2/81 patients; and they responded to the treatment. No difference was noted in terms of outcome between younger (< 5 years) and older children.

Conclusion:

We hereby present the largest Indian cohort of patients with MIS-C. Our study re-emphasizes the need for early diagnosis and timely referral in patients with MIS-C.

Table 1: Demographic and clinical features of patients of MIS-C.

Features	N=81
Age	6.83 yrs
Male	57/81 (70.37)
Female	24/81 (29.6%)
Fever duration	4.65 days
Conjunctival congestion	44/81 (54.3%)
Rashes	44/81 (54.3%)
Gastrointestinal symptoms	43/81 (53%)
Lymphadenopathy	20/81 (24.6%)
Shock	24/81 (29.6%)
Neurological symptoms	8/81 (9.87%)
Low LV Ejection fraction (<50%)	22/81 (27.1%)
Coronary artery abnormalities	8/81 (9.87%)
Treatment with IVIG alone	11/81 (15.3%)
Treatment with steroids alone	9/81 (11.1%)
Treatment with IVIG and steroids	54/81 (66.6%)
Conservative management without steroids and IVIG	5/81 (6.2%)
Average duration of hospital stay	6.6 days

RARE CASE OF INFANTILE KAWASAKI DISEASE PRESENTING AS ASPETIC MENINGITIS

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ABSTRACT

Introduction:

Kawasaki disease (KD) is an acute vasculitis of infancy and early childhood. Incomplete and atypical forms of Kawasaki Disease are now being increasingly diagnosed and reported.1,2 Infants <6 months of age with fever, rash and CSF pleocytosis presents a diagnostic dilemma because the clinical presentation in KD patients may initially resemble other infectious diseases, including bacterial or viral meningitis.3 We hereby present a case of infantile KD with aseptic meningitis.

Case:

A 3 month old male child presented with moderate grade fever spikes, loose stools since 4 days with maculopapular rash over cheeks since 2 days. On examination child had cracked lips, bilateral conjunctival congestion, perianal rash, unilateral left cervical lymphadenopathy and hepatomegaly. Child was started empirically on IV Ceftriaxone, IV Vancomycin with other symptomatic treatment. Suspecting late onset sepsis, CRP, ESR sent were raised while lumbar puncture showed CSF pleocytosis (45 cells with 85% microglial cells). Since high grade fever spikes persisted along with lymphadenopathy, erythema and cracking of lips with CSF pleocytosis clinical diagnosis of Kawasaki Disease with aseptic meningitis was made. 2D Echo showed dilated coronaries and Pro BNP sent was 1787 pg/ml confirming KD. Child was given intravenous immunoglobulin (IVIG) @2g/kg and Aspirin (80mg/kg). Gradually fever spikes reduced, repeat inflammatory markers showed improving trend with normal coronary dimensions.

Conclusion:

As a conclusion, neurologic manifestations like aseptic meningitis may precede in KD. CSF pleocytosis is a common feature of acute KD and occurs in at least one-third of patients. The atypical form of KD seems to predict a higher risk of coronary dilatation; so, a high index of suspicion forts this diagnosis. Prompt recognition of the disease and early initiation of treatment with IVIG results in significant reduction in the occurrence of coronary artery abnormalities with better prognosis.

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Neutrophil NADPH oxidase activity in patients with Kawasaki disease

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ABSTRACT

Introduction:

Kawasaki disease (KD) is a systemic, medium vessel vasculitis. Oxidative stress has an important role in pathology of KD as it triggers of reactive oxygen species (ROS) production. NAD(P)H oxidase complex is the main source of ROS production. The dihydro rhodamine assay (DHR) is done to quantify the functional status of NADPH oxidase system.

Methods:

This study was carried out to do comparative analysis of NADPH oxidase function in KD patients with coronary artery aneurysms (CAAs) with healthy controls. A total of 14 KD patients (Group1: 4 patients diagnosed > 6 months-1.5 years; 2 with persistent, 2 with transient CAA) (Group 2: 5 patients diagnosed >1.5 - 3 years; all with transient CAA) (Group3: 5 patients diagnosed > 3 - 4.5 years; 2 with transient, 3 with persistent CAA) and 14 age matched healthy controls were enrolled.DHR123, used as a substrate for respiratory burst assay, is oxidised to rhodamine by hydrogen peroxide. Rhodamine is a fluorescent dye and can be readily detected and measured on flow cytometer. Auto-fluorescence of cells in FL1 channel was measured for unstimulated cells after loading with DHR dye and fluorescence of dye after reduction due to ROS production upon phorbol myristate acetate stimulation was measured for stimulated cells. Oxidative burst estimation was measured by calculating delta mean fluorescent intensity (ΔMFI= MFI Stim-MFI Unstim) and Stain Index (S.I.) = MFI of Stained cells/MFI of unstained cells

Results:

The ΔMFI of patients was found to be higher (non-significant: Group 1 P=0.05; Group 2 P=0.30; Group 3 P=0.2) as compared to controls. Inflammatory cell migration and infiltration to the arterial wall orchestrate ROS production leading to respiratory burst.

Conclusion:

Oxidative stress has pathogenic role in functional changes of arterial wall. ROS production was found to be enhanced in KD patients with CAA compared to controls; however, this difference was not statistically significant probably due to small sample size.

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Peripheral gangrene in Kawasaki disease: An unusual presentation

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ABSTRACT

Peripheral gangrene in Kawasaki disease: An unusual presentation

Objective:

We report 5 cases of peripheral gangrene in patients with KD which is an unusual manifestation.

Patients and methods:

Records of all children diagnosed to have KD during 1994-2021 were analyzed. Of the 1076 patients with KD, clinical details of children who developed peripheral gangrene were retrieved.

Results:

Out of 1076 patients, 5 patients of KD were noted to have peripheral gangrene. The median age of the children was 14 months with a slight female preponderance (male: female 2:3). All children (100%) had a febrile illness with 2 out 5 (40%) children also presenting with a maculoppular rash all over the body. Shock was the presenting manifestation in 2 (40%) children. Where 2 (40%) children had a pneumonia at presentation, the other 2 (40%) had a gastrointestinal involvement. 1 child (20%) developed macrophage activation syndrome (MAS) post therapy for KD. All children (100%) were noted to have progressive thrombocytosis and elevated inflammatory markers at the time of diagnosis with normal coronaries on 2 D echocardiography. All children were given IVIg at 2g/kg/day, whereas only 3 were started on low molecular weight heparin followed by aspirin. The child with MAS was treated with pulse intravenous methylprednisolone. 1 child was managed with early augmentation of therapy considering the age (2 months) and myoccardial involvement.

Discussion:

There are no well-defined pathogenic mechanisms behind peripheral gangrene in KD but it is believed to be due to vasculitis of the peripheral vessels, thrombosis or vasospasm. Other than the standard treatment for KD these patients may require additional therapy such as heparin, prostacyclin, urokinase, nitroprusside, nifedipine, dipyridamole, propranolol, steroids, cyclophosphamide and infliximab. Despite these measures, prognosis of peripheral gangrene in patients with KD remains guarded and many children need amputation. Early diagnosis and aggressive treatment has been reported to help in salvaging the limb.

Table 1: Demographic and clinical features of patients of MIS-C.

TITLEK	AWASAKI DISEASE PHENOTYPE AND PHENOTYPIC SPECTRUM OF MULTISYSTEM IFLAMMATORY SYNDROME IN CHILDREN-SARS-COV2 ASSOCIATED IN A TERTIARY CARE HOSPITAL IN CENTRAL KARNATAKA
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Peripheral gangrene in Kawasaki disease: An unusual presentation

Authors:

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KAWASAKI DISEASE PHENOTYPE AND PHENOTYPIC SPECTRUM OF MULTISYSTEM IFLAMMATORY SYNDROME IN CHILDREN-SARS-COV2 ASSOCIATED IN A TERTIARY CARE HOSPITAL IN CENTRAL KARNATAKA

ABSTRACT

INTRODUCTION:

Corona virus disease 2019 in children is usually mild but can cause inflammatory syndrome after SARS COV-2 infection. A phenotypic classification of the inflammatory syndrome helps in triaging, prevention of duplication of efforts and effective utilization of resources.

OBJECTIVE: To profile the various clinical manifestation and phenotypically classify MIS-C as per WHO-IAP criteria including KD phenotype.

METHOD AND ANALYSIS:

Descriptive observational study of children admitted with a diagnosis of MIS-C from the ages of 1month to 18 year in a tertiary hospital catering to central Karnataka between March 2021 and August 2021. Each patient underwent clinical and laboratory evaluation and were classified to MISC phenotypes. From each patient we obtained nasopharyngeal swabs to test for SARS COV-2 using reverse transcription-polymerase chain reaction. We also took sample to test for IgG antibodies against SARS CoV-2.

RESULTS:

Out of 400 children admitted to our tertiary care hospital, 80 were suspected of MISC and after exclusion criteria 64 children were proven to be MISC. Febrile inflammatory syndrome was the most common presentation (38cases-4.75%) followed by KD phenotype and toxic shock syndrome. MISC can also present as organ dysfunctional symptoms and signs (6/64). Most of the children presented with history of fever from 2nd to 12th day with mean duration of 5days. 18 children received IVIG infusion and rest were treated with steroid and aspirin. Mean duration of hospital stay was 5 days. All the children are doing well in the short follow up.

CONCLUSION:

Early phenotypic classification could help in management and in effective utilization of resources and finances. A high index of suspicion, early phenotypic classification and team dynamics helped in taking effective decisions and to differentiate between Kawasaki disease and Kawasaki like phenotype.

T cell activation profile in children with Kawasaki disease

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ABSTRACT

Background:

Several studies have implicated CD8+ T lymphocytes in pathogenesis of KD.

Study method: Study was carried out at Advanced Pediatrics Centre, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, India during the period 1st Jan 2018 to 31st July 2020. In this prospective study, we have assessed the lymphocyte activation status in KD (n=10) comprehensively by flow cytometry using both early and late activation markers- CD69 and HLA DR, respectively, and also by measuring soluble CD25 levels in serum by enzyme linked immunosorbent assay (ELISA) during the acute and convalescent stages of the KD. We also compared these activation markers between KD, febrile control (n=9) and healthy control (n=10). Furthermore, we studied the HLADRA and HLADRB gene expression in different subgroups (KD without CAA, KD with CAA and healthy control) and compared amongst them.

Result:

We enrolled 10 children with KD in this study. None had CAAs / IVIg resistance. Flow cytometry revealed a significantly high percentage expression of CD69 in CD3+ and CD3+CD4+ T lymphocytes in KD and febrile controls compared to healthy controls. We also observed a higher expression of CD69 in CD3+CD8+ lymphocytes in KD and febrile controls compared to healthy controls. We found no significant increase in late activation marker HLA DR in CD3, CD3+CD4+, and CD3+CD8+ lymphocytes between KD, febrile, and healthy controls. Soluble interleukin-2 receptor (CD25) assessed by ELISA was significantly elevated in children with KD and febrile controls compared to healthy controls. Longitudinal follow up in children with KD showed a decreasing trend of early activation marker- CD69 in CD3+CD8+ lymphocytes and serum soluble CD25 levels over time. However statistically significant difference was only found in soluble CD25 values. mRNA expression of HLADRA and HLADRB was comparable between children with KD a who had CAAs and those without CAAs.

Conclusion:

Our limited size cohort showed early but not late activation of T lymphocytes in children with KD. Markers of lymphocyte activation do fall with subsidence of systemic inflammation following IVIg therapy in KD.

Key words:

Kawasaki disease, T lymphocytes, CD69, HLADR, soluble CD25

Kawasaki disease as a manifestation of multisystem inflammatory syndrome in association with SARS-CoV2 infection: A prospective study from a tertiary care hospital of North-East India.

Authors:

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ABSTRACT

From:

Dept. of Pediatrics, Gauhati Medical College, Guwahati, Assam, North-East India.

Background:

The multisystem inflammatory syndrome in children (MIS-C) is a potentially serious complication associated with current or past infection with SARS-CoV2. Occasionally patients with MIS-C can present with syndrome similar to Kawasaki disease.

Objective: In this study we report our experience with the patients with Kawasaki disease as a manifestation of MIS-C over one year period.

Methods:

Study design: Prospective study with limited follow-up. Study duration: one year (from 1st September-2020 to 31st August-2021). Study setting: Pediatric Rheumatology Services of Department of Pediatrics, Gauhati Medical College, Guwahati. Inclusion criteria: all patients with MIS-C who had presented with features of KD. Exclusion criteria: patients with MIS-C without the clinical features of KD.

Results: During the study period, a total of 9 patients with MIS-C had manifestations similar to KD. Of these, 9 patients had complete KD. The mean age at presentation was 9±2.4 years. The evidence of COVID-19 in the recent past was present in 1 patient. Abdominal symptoms were present in 7 patients (diarrhea 7, vomiting 1, acute abdominal pain 6). The mean C reactive protein was 215.4±136.54 mg/dL and the mean d-dimer level was 5.12±4.7 ㎍/mL (normal range <0.5 ㎍/mL of FEU). The complications during presentation were, coronary artery abnormalities (CAA) in 2 cases, pericardial effusion in 2 cases, suspected myocarditis in 2 cases and acute kidney injury in 1 case. All patients in our cohort were treated with intravenous immunoglobulin to which there was dramatic response with rapid defervescence. On follow-up all patients were doing well and the patients with CAA had normal coronary artery diameters after 2-4 weeks of follow-up.

Conclusion:

Patients with MIS-C can presents with the features of complete KD and have predominantly abdominal symptoms and a very high levels of CRP. Patients in our cohort were doing well on follow-up.

EPIDEMIOLOGY OF KAWASAKI DISEASE IN COVID TIMES

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ABSTRACT

Background:

There is dearth ofdata on the epidemiology of Kawasaki Disease(KD) in India.

Objective:

Estimate incidence of KD during the two pandemic years and compare it with the pre-pandemic years.

Methodology:

Data of KD patients admitted at the Institute of Child Healthduring the first and second wave of SARS-CoV2 were compared with data from the pre-COVID era.

Results:

1. The first wave(March 2020- December 2020): 33 KD cases, 18 females and 15 males.
   The second wave(April 2021 - July 2021): 13 KD cases, 4 females and 9 males.
2. In the pre-COVID era, the incidence of KD was:
   a. 2018: total cases 36, females 11 and males 25
   b. 2019: total cases 39, females 14 and males 25
   There was a rising trend of KD every year with cases doubling in number from 18 in 2009 to 39 in 2019.
3. First wave had 33.33% cases and the second wave had 61.54% cases with coronary dilatations but no giant aneurysms (z score> +10) were seen during either waves. In comparison, in 2018 16.67% cases had coronary involvement with giant aneurysms in 2.78% and in 2019 30.77% cases had coronary involvement with giant aneurysms in 5.13%.
4. The first wave had 75 cases of MISC, with 22 (29.33%) KD phenotypes. The second wave had 48 cases of MISC, with 23 (47.9%) KD phenotype. The second wave of MISC had a greater proportion of younger children (median age 6.6 years) with doubling of the KD phenotype.

Conclusion:

1. Incidence of KD was similar to that of the preceding years, following the same upward trajectory despite the lockdown.
2. If the KD phenotype of MISC is taken into account, there was a 2 fold increase in the incidence of KD-like illnesses.

Subhajit

Case Abstract: Infantile Kawasaki disease with giant coronary arterial aneurysms

An eight months follow up for an infant with Kawasaki disease with giant coronary artery aneurysms

Authors:

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ABSTRACT

A 33 days old male child presented with history of fever which was associated with diffuse erythematous rash all over the body on day 2 of fever, which resolved spontaneously after few days. He was suspected to have late onset neonatal sepsis and was given with intravenous antibiotics in an outside hospital for 11 days. However as there was no improvement, the child was referred and came to our center.

On evaluation the child has, leukocytosis, thrombocytosis and mild anemia. ESR was 95, hsCRP was 4.18mg/L. The child was continued on broad spectrum antibiotics however fever persisted. Blood, urine and CSF cultures were sterile. On day 5 of hospital stay (day 16 of illness), the child was noted to have erythema of lips and tongue, periungal peeling of skin of hands and feet. The child also has elevated ferritin, triglycerides and sterile pyuria. Echocardiography revealed gaint aneuryms of left main(LM), left anterior descending(LAD,) right coronary arteries(RCA), (LM 5.33mm, +13.5 Z, LAD prox 3.8mm, +10.19 Z, RCA 3.85mm, +10.4 Z) Anti SARS-COV2 antibody was negative. Hence the diagnosis of Kawaski disease with giant coronary artery aneuryms was made. Antibiotic was stopped and the child was started on IVIG 2g/kg and aspirin 50mg/kg/day and enoxaparin 1mg/kg twice daily. 48 hours after the child became afebrile, aspirin was decreased to 5mg/kg/day, and was continued on low dose aspirin and enoxaparin after discharge.

Regular follow up with echocardiography for the past 8 months did not reveal any significant increase in the sizes of the coronary aneurysms. There was no thrombotic or bleeding complications during the follow up period.

Conclusion :

Kawasaki disease should be considered early as a differential diagnosis in children with persistent fever and mucocutaneous lesions. Low molecular weight heparin (Enoxaparin) appears to be a safe and viable option for long term thromboprophylaxis in infants with giants coronary aneurysm where regular INR monitoring and warfarin dose adjustment may not be feasible.

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